



# THE HIV/AIDS NEWSLETTER

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A Quarterly Newsletter from Y. R. Gaitonde Centre for AIDS Research and Education

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## From the Director's Desk

It gives me great pleasure to release the inaugural issue of "The HIV/AIDS Newsletter" from Y. R. Gaitonde Centre for AIDS Research and Education (YRG CARE).

YRG CARE began its services in the year 1993. Over the years, it has gradually shaped a comprehensive response to the HIV/AIDS challenge. Not a week goes by without new strides in HIV research. This quarterly newsletter is aimed at providing both the medical and scientific fraternity an opportunity to touch base with the recent developments in this field.

We hope that this newsletter and those that follow would be of assistance to investigators, in making informed decisions on therapy and experimental approaches. We solicit your comments and suggestions for further improvement.

Sincerely,

**Prof. Suniti Solomon, MD.**  
Editor-in-chief

## MINIREVIEW

### Clinical Research

## Can We Sustain the Decline in Morbidity and Mortality Due to HIV Following Highly Active Antiretroviral Therapy in India?

By *Dr. N. Kumarasamy*

Since the first report of HIV in India in 1986 [1] this infection has been documented from many parts of India. Currently it is estimated that there are 2 to 3 million persons living with HIV in India [2]. More than 80% of persons diagnosed with HIV in India have one or more opportunistic infections, of which, tuberculosis is the most common [3, 4]. Due to the absence of a true seroconversion cohort in this country, it is hard to describe the natural history of HIV infection. Studies have shown that the mean survival time from sero-diagnosis is 92 months [4]. Tuberculosis, PCP, cryptococcal disease and HCV coinfection act as cofactors for HIV disease progression. Patients who have at least one opportunistic infection progress 2.6 times faster than those who do not. Antiretroviral therapy in patients even with low CD4 lymphocyte counts improves the odds of survival. From this evidence it is clear that preventing, diagnosing and managing opportunistic infections should be given priority. Efforts should be made to create more and more user-friendly VCT centers to identify HIV infected individuals in the early course of the disease.

Antiretroviral drugs were first introduced in India by generic manufacturers in 1993. Combination fixed dose antiretroviral drugs were launched in 1999. The cost of first line HAART in India was Rs. 25000 per patient per month in the year 1998 and it reduced to less than Rs.1000 in 2005. Effectiveness of generics were questioned earlier, but the studies conducted in India using generic ARVs showed that these drugs were safe, tolerable, efficacious and effective [5 - 7]. Due to the cost reduction of these generic ARVs, there is an increased access to ARVs in India and in other developing countries. The Government of India launched the ARV roll out program through the tertiary government hospitals in India in April 2004. Since then around 50,000 patients have been receiving ARVs in the public sector and nearly 40,000 in the private sector. Recent studies have shown that the generic HAART has made a huge impact on changing the natural history of HIV disease in India and also has lead to dramatic reduction in HIV related morbidity and mortality [8, 9]. Still many numbers of HIV infected patients in India who need HAART don't have access to ARVs. Are we denying survival benefits to them due to access?

Second line protease-inhibitor-containing ARVs are also manufactured by Indian generic companies but cost 5 - 8 times the price of the first line drugs [10]. This huge price disparity will be a major concern for the Indian patients when they fail the first line ARVs in terms of access. Are we controlling disease progression on a long run?

Cost and stigma are the major co-factors for poor adherence to ARVs in India [11, 12]. Many of the Indians live in a nuclear family. Still HIV infection has a huge stigma in India. Studies have shown that people who had not disclosed their HIV status to their household members reported poor adherence to ARVs. This is due to stigma. Efforts should be made to remove HIV related stigma from the community still for improved survival due to ARVs.



Adverse events and immune reconstitution syndrome (IRS) among persons who are co-infected with tuberculosis and initiated on HAART [13] are major issues, which can lead to discontinuation of ARVs. Adverse events are one of the major reasons for modifying first line HAART in resource limited settings [14]. Importance of clinical and laboratory follow-up should be stressed at each visit to identify early toxicities to HAART. On-going training for physicians is a must.

Mutations to ARVs are reported from India in the naïve population [15, 16]. Due to the fact that Indian HIV-infected patients experienced mono and dual therapy in the earlier years and also due to the improper prescriptions of ARVs from untrained physicians in HIV medicine, India might face a threat of MDR HIV strains! Efforts should be made to prevent this. Due to increased numbers of HIV infected persons needing HAART and also due to increased access to ARVs, immediate efforts should be made to train physicians on antiretroviral therapeutics.

Due to the high cost of viral load, CD4 monitoring is the standard of care in developing countries and recommended by guidelines for resource limited settings. Due to this fact, patients who fail virologically continue the failed 1<sup>st</sup> line HAART until immunological failure, which can lead to accumulation of drug-resistant variants in those patients. A study conducted at our institution enrolled 3739 patients who initiated AZT/d4T+3TC+NVP/EFV containing 1<sup>st</sup> line HAART. Median CD4 at the initiation of HAART was 100. Among them, 336 (9%) switched to 2<sup>nd</sup> line HAART as per immunological failure definitions of WHO guidelines. The median CD4 at the time of switch was 196 and the median duration on 1<sup>st</sup> line before switch was 3.7 yrs. Among them, 62 patients who were on 1<sup>st</sup> line HAART for a duration of 2.7 yrs were screened for drug-resistant HIV strains. Seventy-nine percent of the patients were infected with HIV carrying the M184V mutation, 82 % with NNRTI-resistant HIV; 42% with TAMs, 14% with Q151M, 5% with K65R and 3% with L74V resistant HIV. This data clearly warns that patients with immunological failure with standard WHO criteria have severe mutations, which can jeopardize future 2<sup>nd</sup> line NRTI options. Hence there is an urgent need for low cost viral load in resource limited settings for monitoring persons with HIV who are on HAART to avoid severe mutations and to protect future options for therapy [17].

A recent study has indicated that antiretroviral therapy will lead to major survival benefits and is cost effective. The findings showed HAART if initiated before the CD4 counts reach 250 cells would have a dramatic effect on survival and be very cost effective. The availability of second-line regimens will further increase survival but their cost effectiveness would depend on their relative cost when compared with first line regimens [18]. Hence, to sustain the decline in morbidity and mortality due to HIV, following highly active antiretroviral therapy in India, can we have cost effective viral load and cheaper second-line antiretrovirals?

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## MINIREVIEW

### Basic Science / HIV Vaccines

# HIV: Scientific Roadblocks on the Runway to an Effectual Vaccine

By *Dr. E.M. Shankar*

Despite significant advances in drug therapies that have provided increased endurance for the HIV-infected individuals with easy access to medications, HIV infections and AIDS-related deaths are increasing at an overwhelming rate in third-world nations particularly in Asia [1]. Long-term treatment with multiple drugs is quite impracticable due to inadequate healthcare resources and infrastructure. Notwithstanding the fact that extensive research has gone into unraveling the etiology and pathogenesis of HIV, the development of a successful vaccine continues to present an inimitable challenge to the scientific community [2] for more than 25 years since the discovery of HIV. The reason could be the unpredictable nature of the viral immunopathobiology that continues to present considerable impediment to vaccine development [2, 3]. Unique features of HIV have rendered habitual vaccine approaches ineffective. Thus, almost three decades since its discovery, we are still in anticipation of an effectual HIV vaccine.

## Need for a vaccine.

The hallmark of HIV-1 infection lies in its propensity to drain CD4+ T cells, a particular subset of immune cells that orchestrates all types of immune responses against pathogens, which consequently leads to foreseeable morbidity and mortality due to opportunistic infections and neoplasms. A partially-effective AIDS vaccine that could help bolster the immune response against HIV before too many CD4+ T cells are damaged might help preserve the pool of critical immune cells early in the course of infection and significantly slow disease progression. Such a vaccine in addition, may also reduce the likelihood of an infected individual transmitting HIV to others. Therefore, development of at least a partially effective vaccine that can prevent deterioration of the immune system can have a potent effect on the epidemic.

## HIV genome vs host immune repertoire.

The prime incomprehensibility in developing an effective HIV-1 vaccine is the marked genetic variability of HIV-1 [4]. Once HIV infects a CD4+ T cell, it quickly produces more viruses than it can subsequently infect more immune cells, setting off a cycle of destruction that allows HIV to overwhelm and eventually destroy the immune system. But this replication process is often defective and each time HIV copies its genetic material it makes mistakes (mutations). Mutation events that occurs during the course of HIV disease results in the expression of complicated 'newer' antigenic motifs which in turn leads to host 'immunological confusion' within the immune arm repertoire. This subsequently results in the escape of the virus from the immune components that effectively enhance the magnitude of viral replication.

Auxiliary diversity arises in response to immune pressure, either by HIV-1-specific antibodies or by CD8+ cytotoxic T cells (CTLs). Together, these events lead to ~10% genetic alteration in an infected individual over the course of infection. Twenty to 30% differences exist in the nucleotide sequences of HIV envelope genes (*env*) in the HIV-1 subtypes that account for the global epidemic. Thus, the development of one global vaccine that can protect against all HIV-1 subtypes may be challenging.

## Escape from neutralizing responses.

Neutralizing antibodies (nAb) are antibodies that can bind to the gp120 spikes of HIV-1 and prevent them from binding to the CD4+ receptors of host CD4+ T cells. Although many types of HIV-specific antibodies are produced by the humoral immune system, very few are capable of binding and neutralizing the virus. These select few antibodies called nAbs can successfully stop the virus



from infecting cells [4]. NABs that can effectively neutralize many different strains of HIV are called broadly cross-reactive nABs. These are very rare and so far only a handful have been identified. HIV adopts several ways to protect itself from being neutralized by nABs. One is that the virus can mutate very rapidly, which could cause a slight change in the virus's shape or structure.

Most HIV-infected individuals produce HIV-specific antibodies soon after becoming infected. But even in the short amount of time it takes for the adaptive immune system to gear up and start producing HIV-specific antibodies, the virus can alter itself so dramatically that the antibody no longer recognizes the majority of the protein domains of the virus, which renders nABs ineffective. Furthermore, the viral gp120 itself is coated in bulky and unevenly folded sugar molecules [5] (heavily glycosylated, while passing through the golgi complex) that act as a shield, effectively blocking the antibodies from reaching their target (gp120). Glycosylation enables flexibility of the polysaccharide motifs leading to strain variations in Env domains, again favouring neutralization escape [5]. And even when nABs are generated, they are sometimes inept enough to protect against other closely related strains of the virus [6].

There are several confirmed cases of superinfection, where HIV-infected individuals have been infected with a second strain of HIV despite having antibodies towards the strain that they were already infected with. In addition, despite the fact that several HIV-specific nABs have already been discovered in infected individuals, it is still unclear how effectively they clear infection. There has never been a documented case of a person who was able to clear an established infection by nAB responses. Another way to assemble useful information about the types of immune responses that protect against infection is to study the virus in an animal model. But the simian immunodeficiency virus (SIV) that infects rhesus macaques is not a perfect model for human infection since it is a different virus and any vaccine candidates that are tested in non-human primates are often based on SIV and not HIV.

The potentially neutralizing monoclonal antibodies (e.g. 4E10, 2G12, b12, 2F5 etc.) generated by vaccinologists from bone marrows of HIV+ patients' critical conserved epitopes like the CD4-BS, CD4-I and variable loop epitopes may be useful, but the presentation of these epitopes in context to a vaccine may be challenging [1]. Furthermore, the vulnerability of HIV to interference (point mutations) within the membrane-proximal external region (MPER)-specific MAbs calls for a further evaluation of the safety and efficacy of MPER-targeting therapeutic and vaccination strategies [6].

### Any hope left?

The key to inducing competent immune responses with a vaccine is selecting the right immunogen either whole HIV proteins or pieces of protein that will stimulate the immune system to induce the preferred type and amount of responses. Designing immunogens for AIDS vaccines is often tricky and only incremental progress has been made in this quarter. Currently several different immunogens are being evaluated in both pre-clinical and clinical trials. These immunogens are being tested in combination with several different viral vectors to boost the level of immune responses that are generated.

Other approaches to perk up the immunogenicity of vaccine candidates can also be attempted, including alternative delivery methods—such as intravenous, oral, or intra-nasal administration. Furthermore, even though antibodies may not play a critical role in controlling HIV, researchers speculate that vaccine-induced HIV-specific antibodies would still be important, even necessary, in protecting against infection. This presents a significant challenge to vaccine researchers who have to discover novel ways to induce immune responses that are even more effective than those produced during natural infection.

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## RESEARCH COMMENTARY

### HIV Diagnostics

## Use of Plasma Preparation Tube for HIV-1 Plasma Viral Load Testing: Does it Work?

**Original Article:** García-Bujalance, *et al.* Elevation of viral load by PCR and use of plasma preparation tubes for quantification of HIV-1. *J Microbiol Meth* **2007**; 69: 384 - 386.

**Summary.** The purpose of this study was to evaluate whether plasma preparation tube (PPT) can be used for HIV plasma viral load (PVL) testing without compromising the quality of laboratory results. The study compared the viral load results (n=51) from plasma stored in primary PPT (plasma *in situ*) and PPT plasma specimen transferred into secondary transport tubes before freezing. The specimens were processed for HIV-1 viral load testing using the Roche Amplicor HIV-1 MONITOR, version 1.5 with ultra-sensitive method. The authors concluded that freezing the primary specimen tube can falsely elevate PVL and they recommended the transfer of plasma specimen from primary tube before freezing.

**Commentary.** Levels of HIV-1 RNA in plasma as a virological marker have been found to be a very useful marker of prognosis, disease progression and efficacy of antiretroviral therapy and can be used primarily to make decisions effectively to initiate or change antiretroviral therapy [Simone, EL, *et al.* 2007]. Therefore, the accurate and reliable quantification of PVL is an essential part of the management of HIV disease. However, the major hurdle in using PVL in resource-limited settings is the cost and logistics involved in shipping the specimens to testing laboratory. But the cost of PVL is becoming lower by use of alternative technologies [Balakrishnan, *et al.*, 2005; Rouet, F, & Rouzioux, C, 2007]. The BD Vacutainer PPT was evaluated by several investigators to determine the effects of various handling and shipping conditions on PVL.

The PPT (K<sub>2</sub>EDTA) is a plastic evacuated tube and contains a polyester material, which separates cellular materials away from the supernatant, plasma (centrifugation should be done within 2 hours of blood collection). The advantages of PPT are convenient, safe, decreases risk of errors, single-tube system for the collection of whole blood and the separation of plasma without opening. The PPT can be transported *in situ* thereby reducing the possibility of exposure to blood-borne pathogens at the collection and specimen processing sites.

The authors report that PPT is very convenient for collection and transportation to the testing laboratory, but the freezing of the plasma specimen in primary PPT can elevate HIV-1 PVL particularly with the low viral load (<1000 copies/mL) and these findings are also supported by other investigators [Salimina, *et al.*, 2005; Griffith & Mayo, 2006]. The impact of variability at the low PVL is significant for the interpretation of transient viral load changes in clinical practice. However the studies with the higher viral load specimens showed no significant differences between standard EDTA tubes and PPT [Holodniy, *et al.*, 1995 & 2000; Mallen, *et al.*, 1999]. The elevation in low-level of PVL may be associated with the HIV release from platelets (plasma prepared in a PPT may contain a higher concentration of platelets than that found in whole blood) in to the plasma during thawing [Sabino, *et al.*, 2004].

Generally HIV-1 PVL assays allows the storage of separated plasma for 24hours at ambient temperature (<25°C), 5 days at 2-8°C or frozen indefinitely without compromising the quality. Therefore, the specimen collected in PPT can be transported to the testing laboratory with wet ice or gel pack shipment. This collection system is very useful particularly for places which do not have facilities to separate plasma specimens or ship frozen plasma on dry ice.

By Dr. P. Balakrishnan



## RESEARCH COMMENTARY

HIV Basic Science

### Pharmacogenomics and Antiretroviral Therapy

**Original Article:** Haas, *et al.* Pharmacogenetics of long-term responses to antiretroviral regimens containing efavirenz and/or nelfinavir: an Adult AIDS Clinical Trials Group Study. *J Infect. Dis.* **2005**;192: 1931 - 1942.

**Summary.** Adult AIDS Clinical Trials Group study 384 examined associations between host genetic variants and long-term responses to treatment of 504 randomized antiretroviral-naive subjects to receive efavirenz and/or nelfinavir plus 2 nucleoside analogues, with follow-up lasting up to 3 years. Of the participants, 49% were white, 31% were black, and 19% were hispanics. They found plasma exposure to efavirenz and nelfinavir in each population was significantly associated with the polymorphisms, MDR1 position 3435 TT in efavirenz recipients and CYP2C19 681G-->A nelfinavir recipients was associated with decreased likelihood of virologic failure and decreased emergence of resistant virus.

**Commentary.** Globally, the pharmacogenomic knowledge base is likely to be of considerable importance in helping to anticipate complications of antiretroviral drug treatment in ethnic populations that may not have been well represented in clinical trials. In the very near future such mechanisms, called 'cellular drug resistance', might be taken into account, together with other immunological, virological and behavioural factors, to explain 'drug failure' and/or the variability of response in HIV patients undergoing antiretroviral treatment. With the expanding number of antiretroviral compounds and the requirement for lifelong treatment of HIV-1-infected persons with antiretroviral agents, both viral and cellular resistance must be considered in the context of failing chemotherapy.

By Dr. S. Saravanan

## RESEARCH HIGHLIGHTS

### Drug Resistant HIV may Revert to being Sensitive in the Blood but Not in the Genital tract!

*The Journal of Infectious Diseases 2007;196: 356 - 360*

During HIV infection, the male genital tract (MGT) acts as a viral nidus with restricted gene flow and a slow molecular clock. This allows for the possible development of drug resistance, its long-lived persistence, and subsequent transmission. Once transmitted, the drug-resistant variant reverts very slowly, over the course of years, to a drug-susceptible phenotype in blood.

A study conducted in University of Washington, Seattle demonstrated that prolonged persistence in the MGT could contribute to the high prevalence rates of transmitted drug resistance. The study was carried out in 5 individuals (MSMs) newly infected with HIV strains, which were genotyped as NNRTI-resistant. In 3/5 participants, NNRTI resistance persisted in both blood and semen throughout follow-up (444 days after estimated date of infection (EDI)). In the other two, drug-sensitive strains could be demonstrated in blood >800 days after the EDI. Drug-sensitive virus K103N was detectable in blood but not in semen 875 days after the EDI in one member. Similarly, another individual had a mixture of resistant and wild-type sequences (K103N/K and Y181C/Y) 1179 days after the EDI in blood, but only drug-resistant sequences were detected in semen.

### Hide-out during HAART Exposed

*Journal of Immunology 2007; 178: 6581 – 6589.*

One of the greatest impediments to eradicating HIV in the body and therefore finding a cure for AIDS is viral latency—the ability of HIV to lie dormant in a very small number of cells, invisible to the immune system and resistant to the effects of antiretroviral drugs.

Prof. Suzanne Crowe, at the Burnet Institute in Melbourne, Australia, recently identified a new source for this persistence of HIV in latent reservoirs during HAART. In contrast to the vast majority of monocytes (that are CD14<sup>high</sup>CD16<sup>-</sup>), a minor CD16<sup>+</sup> monocyte subset preferentially harbors HIV-1 in infected individuals on HAART. Also, unlike the majority of monocytes, this subset possesses high molecular mass complexes of apolipoprotein B mRNA-editing enzyme, catalytic polypeptide-like 3G (APOBEC3G) similar to those observed in highly permissive T cells. This forms a continuing source of viral persistence during HAART.

### Repeating Measles Vaccination in HIV Infected Children

*The Journal of Infectious Diseases 2007;196: 347-355.*

A study conducted by Dr. William Moss MD MPH at John Hopkins School of Public Health revealed that HIV infected children could be susceptible to measles because of their waning immunity. Only 50% of HIV-infected children that survived without ART were found to maintain protective antibody levels 27 months after receiving measles vaccine, compared to 89% of children that were not HIV infected. However, 92% of HIV-infected children who were revaccinated showed protective antibody levels. Additional research should be conducted to determine the duration of measles immunity in HIV-infected children receiving ART and their response to revaccination against measles.

### Molecular HIV Clipper

*Science 2007;316: 1912 - 1915.*

The basic biology of HIV-1 requires that it reverse transcribes its RNA genome into cDNA and then dsDNA in order to integrate into the host chromosome and persist there as a provirus flanked by long terminal repeats (LTRs).

Indrani Sarkar and Ilona Hauber from the Max Planck Institute for Molecular Biology and Genetics, Germany reported a novel strategy to rid cells of HIV infection. A recombinase "Tre" was genetically tailored to identify an asymmetric sequence within HIV-1 LTR. This enzyme efficiently excised integrated proviral DNA from the genome of infected cells. This breakthrough could form the basis of development of future vaccines.

### First Report of a HIV-1 Clade C Seronegative Case!

*Clinical Infectious Diseases 2007;45: 69 - 70.*

With the high sensitivity of currently used HIV diagnostic test kits, false negatives would be least expected. The "window period" is the only acceptable phase of seronegativity. However, Novitsky *et al.* (2007) recently reported a strange case of persistently antibody-negative HIV-1 subtype C in Botswana, which was detected during screening for acute infection. The patient denied any high risk behavior in the past 6 months. She was proven to be HIV infected by clinical parameters, CD4 counts and plasma viral load with >750,000 copies/mL (RT-PCR), but was consistently negative by ELISA and western blot tests. The possibilities of recombinant forms and agammaglobulinemia were ruled out by phylogenetic analysis of viral genome and immunoglobulin profile



## HIV-1 Entry Blocking Potentials of Green Tea Identified!

*The Journal of Immunology 2007;178: 47.18.*

Green tea or "true tea" undergoes minimal oxidation during processing of tea leaves and is widely known for its medicinal properties. Besides being a cholesterol lowering agent and a rich source of antioxidants, green tea has recently been reported to possess anti-HIV properties *in vitro* attributable to its polyphenolic rings by means of which it binds to a variety of molecules. A research team at Baylor College of Medicine, Houston demonstrated that epigallocatechin gallate (EGCG); a green tea flavonoid has HIV blocking potentials. Physiologically relevant concentrations of EGCG reportedly prevent binding of gp120 to human CD4+ T cells. Binding studies using spectroscopy and flow cytometry revealed that EGCG competes with gp120 of HIV-1 for occupying the CD4 binding pocket. This competitive binding property of EGCG may pave way for future HIV-1 entry blockers.

## Fish Oil: Does it Control Dyslipidemia in HIV Patients?

*HIV Medicine 2007; 8: 346 – 356.*

HIV infected patients treated with HAART usually develop abnormalities in their lipid metabolism. Scientists at the University of British Columbia, Canada conducted a comparative study on the effects of prescription drugs/ fish oil on dyslipidemic patients. A total of 237 patients were included in the study. They were differentiated into the following categories (1) no treatment (2) statin treatment (3) fibrate treatment (4) thiazolidone treatment (5) fish oil treatment and a combination of (2) and (5). Statins appeared to be the only agent that was significantly associated with a reduced total cholesterol concentration; fibrate treatment was associated with the largest reduction of triglyceride concentration, followed by fish oil. But, despite the lowering of blood lipids with drug and fish oil therapy, a majority of patients still had elevated concentrations even after 6 months.

## NRTI Sparing Therapy Improves Immunological Efficacy

*HIV Medicine 2007; 8: 171 - 180.*

Treatment guidelines recommend starting ART with a combination of 3 drugs including 2 NRTIs with either a PI or a NNRTI. Resistance mutations generally confer cross resistance to NRTIs. Use of NRTIs has also been discouraging because of toxicity and tolerability issues. Toxicity has been ascribed to NRTI inhibitory activity on DNA  $\gamma$ -polymerase and induction of mitochondrial dysfunction resulting in hyperlactemia and a large spectrum of illnesses that comprise peripheral neuropathy, myopathies, steatohepatitis, pancreatitis, lipoatrophy, renal tubular acidosis, postnatal encephalopathy and lactic acidosis. Calmy *et al* recently analyzed pooled data from cohorts treated with NRTI-sparing regimens (NNRTI+ 1PI; NNRTI + 2PIs; 2PIs; 1PI) from Australia and France. Reasons for shifting most patients to this regimen were virological failure/ toxicity due to NRTIs. Immune restoration was satisfactory with the new regimen and virological control was better in pre-treated patients. However, the rate of discontinuation was 41%. This was assigned to either virological failure or the development of an atherogenic lipid profile which occurred at a higher rate in the PI + NNRTI treated group than in the PI treated group.

## CLINICAL TRIALS

## New Microbicide (SPL7013 Gel) Study Launched

The Microbicide Trials Network (MTN) is leading the NIH-funded study in which SPL7013 Gel, or VivaGel™ is being tested for the first time in sexually active young women to determine the product's safety, acceptability and ease of use. VivaGel is thought to act by hampering the ability of HIV to attach to and infect healthy cells. The active ingredient of VivaGel belongs to a class of compounds called dendrimers. MTN-004 is the first of three MTN trials expected to be launched this year. The results, which are expected in 2009, will indicate if the candidate microbicides helped prevent HIV infection in these women (<http://www.mtnstopshiv.org/?q=node/373>).

## Death of US Patient Stirs Unrest over AAV Vaccine Vectors

On July 24, 2007 the U.S. Food and Drug Administration (FDA) was informed by Targeted Genetics Corporation of Seattle about the demise of a patient who received an investigational gene therapy product in a clinical trial for the treatment of active inflammatory arthritis. The recombinant adeno-associated virus (AAV) derived vector was designed to deliver a gene for Tumor-Necrosis Factor receptor, with the intent to inhibit inflammation. Gene therapy was administered into the joint affected by the disease to reduce inflammation in patients with active inflammatory arthritis. Concern has been raised because the HIV vaccine under trial in India is also AAV vector based. However, FDA is not aware of similar adverse events occurring in other gene therapy trials either with this specific product or with those that use other genes in AAV vectors. (<http://www.fda.gov/bbs/topics/NEWS/2007/NEW01672.html>)

## HIV/STD Guidelines *New*

**CDC (US) - Updated recommended treatment regimens for gonococcal infections and associated conditions - United States, April 2007.**

Available at <http://www.cdc.gov/STD/treatment/2006/GonUpdateApril2007.pdf>

**Guidelines for use of antiretroviral therapy for HIV infected individuals in India. API ART guidelines 2007.**

Available at <http://www.japi.org>

**HIV treatment guidelines (past and current information)**

Available at <http://aidsinfo.nih.gov>

**NIH (US) - Entecavir in hepatitis B virus (HBV)/HIV co-infected patients, 2007. Supplement to the guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents (October 2006).**

Available at <http://aidsinfo.nih.gov/contentfiles/EntecavirInHIV.pdf>

**Recommendations for screening, treatment of STIs during pregnancy 2007**

*Am Fam Physician 2007;76: 265 - 270.*

**WHO - Guidance on provider-initiated HIV testing and counseling in health facilities - A new recommendations aim for wider knowledge of HIV status and greatly increased access to HIV treatment and prevention, 2007.**

Available at [http://www.who.int/hiv/pub/guidelines/9789241595568\\_en.pdf](http://www.who.int/hiv/pub/guidelines/9789241595568_en.pdf)

**WHO (SEARO) - Laboratory guidelines for enumerating CD4 T lymphocytes in the context of HIV/AIDS, 2007.**

Available at [http://www.searo.who.int/LinkFiles/AIDS\\_HLM-392.pdf](http://www.searo.who.int/LinkFiles/AIDS_HLM-392.pdf)



## FUNDING OPPORTUNITIES FOR HIV/AIDS

### AIDS International Training and Research Programme (D43)

<http://grants.nih.gov/grants/guide/pa-files/PAR-07-348.html>

### Bill & Melinda Gates Foundation Grants

[www.gatesfoundation.org/ForGrantSeekers/](http://www.gatesfoundation.org/ForGrantSeekers/)

ICMR <http://www.icmr.nic.in/thrust/thrustecd.htm#HIV/AIDS>

GFATM Round 7 <http://www.theglobalfund.org/en/apply/call7/documents/>

NARI-Exchange of Knowledge and Reagents through the "Virtual Knowledge and Resource Center for Reagents, Protocols and Technology" <http://www.hiv-vkrc.org>

### NICHD-Men's Heterosexual Behavior and HIV Infection (RO1, RO3, RO21)

[http://grants.nih.gov/grants/guide/search\\_guide\\_results.htm](http://grants.nih.gov/grants/guide/search_guide_results.htm)

### NIMH R01 Recent HIV Infection: New Prevention Challenges and Opportunities

<http://grants.nih.gov/grants/guide/pa-files/PA-07-087.html>

### Microbicide innovation programme III

<http://grants.nih.gov/grants/guide/rfa-files/RFA-AI-07-034.html>

### A Systems Biology Approach to Infectious Diseases Research

<http://www.fbo.gov/spg/HHS/NIH/NIAID/BAA%2DNIH%2DNIH%2DNIH%2DDMID%2D08%2D22/Attachments.html>



Dr. Charlie Gilks (Director - WHO ART Programme) during his visit on June 27<sup>th</sup>, 2007 congratulated the students of Anna University, Chennai for conducting HIV prevention programmes.

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## Upcoming Events

### 2007/08

#### November' 07

31<sup>st</sup> National conference of Medical Microbiologists; Indian Association of Medical Microbiologists; Nov 16-18; Dr. T.M.A. Pai International Convention Center; Mangalore.  
<http://www.microcon2007.com/static/index.htm>

Global Summit on AIDS and the Church; Saddleback church; Nov28 to Dec1; Lake Forest, California, USA.  
[\[http://www.purposedriven.com/en-US/HIVAIDSCommunity/GlobalConference/Initiative.htm\]](http://www.purposedriven.com/en-US/HIVAIDSCommunity/GlobalConference/Initiative.htm)

Under African skies, the Imagination of Poetry and Storytelling in the HIV/AIDS Pandemic; Community Focus Group (CFG); Nov 29-Dec1; Nairobi, Kenya. [charliecvm@yahoo.com]

#### December' 07

National HIV Prevention Conference; Centers for Disease Control and Prevention; Dec2-5; Hyatt Regency and Atlanta Marriott Marquis, Atlanta, Georgia, USA. [<http://www.2007nhpc.org/backgroundinfo.asp>]

Second National Bioethics Conference; IJ of Medical Ethics; Dec 6-8; NIMHANS convention centre; Bangalore, India. [<http://nbc.ijme.in/>]

East African Conference on the Role of Future Health Professionals on Community based HIV/AIDS control; East African Medical and Pharmaceutical students; Dec 11-15; Butare, Rwanda.  
[\[http://www.medsar.org/conference.htm\]](http://www.medsar.org/conference.htm)

International Symposium on Tropical Medicine and Hygiene; Aga Khan University/RSTMH/IDSP; Dec12-15; Karachi, Sindh, Pakistan.  
<http://www.aku.edu/news/seminars/rstmh/>

Indian Immunology Society, 34<sup>th</sup> Annual Conference; NARI; Dec 16-18; Pune, India. [<http://www.immcon-nari.org/>]

#### January' 08

International Conference on Opportunistic Pathogens in AIDS (ICOPA); All India Institute of Medical Sciences; Jan 27-29; New Delhi, India. [<http://www.icopa-india.org/invitation.htm>]

#### February' 08

15th International Union against Sexually Transmitted Infections; Asia Pacific Congress Dubai; Feb 3; UAE. [<http://www.iusti.ae>]

3rd Africa conference on sexual health and rights; Action Health Incorporated; Feb 4-7; Abuja, Nigeria. [<http://africasexuality.org/>]

## YRG CARE

### Forthcoming Academic Programmes

#### PhD Programme

Applications for PhD programme (affiliated to the University of Madras) at YRG CARE are invited from candidates who have completed their Post Graduate degree in Medical Microbiology/Applied Microbiology/Molecular biology/Biotechnology. Applicants should have passed the national entrance tests for independent fellowships under CSIR /ICMR/ DBT.



## Chennai ART Symposium (CART 2008)

YRG CARE is conducting a 2 day symposium on 11<sup>th</sup> and 12<sup>th</sup>, January 2008 for clinicians involved in HIV care, and for young clinicians who are keen to learn about HAART. The symposium will be conducted by world-renowned clinicians and researchers. Venue: Chennai; Registration fees: Rs.1500 for delegates and Rs.1000 for students. Those interested to participate may contact the organizing secretary – Dr. N. Kumarasamy (kumarasamy@yrgcare.org) and the coordinator Mr. K. G. Kosala Raman (kosal@yrgcare.org).



### Fellowship in HIV Medicine

Applications are invited from eligible candidates for "Fellowship in HIV Medicine" programme - Batch 3.

This programme is a professional "hands-on" HIV disease management training for medical graduates/post graduates, who are interested in acquiring expertise on HIV disease management and diagnostic strategies. The fellowship is a 3-month programme and is offered with stipend. The curriculum involves comprehensive training on the following subjects - Epidemiology and basic science of HIV, Natural history and pathogenesis of HIV, Laboratory diagnosis of HIV, Opportunistic Infections (OI's), Anti-retroviral Therapy (ART), Prevention of Parent to Child HIV Transmission (PPTCT), Post Exposure Prophylaxis (PEP), Sexually Transmitted Infections (STIs) and their laboratory diagnosis. The training will be conducted at YRG CARE medical centres in Chennai. For more details, please contact kosal@yrgcare.org. The last date for applications – 15<sup>th</sup> October, 2007. Applications may be submitted online at <http://www.yrgcare.org/fellowshipform.htm>

## YRG CARE

### Recent Publications

**A randomised control trial of structured interrupted generic antiretroviral therapy versus continuous therapy in HIV-infected individuals in Southern India.** Kumarasamy, N, Flanigan, TP, Vallabhaneni, S, Cecelia, AJ, Christybai, P, Balakrishnan, P, Yephthomi, T, Solomon, S, Carpenter, CC, Mayer, KH. *AIDS Care*. 2007; 19: 507 - 513.

**A social cognitive model of health for HIV-positive adults receiving care in India.** Tarakeshwar, N, Srikrishnan, AK, Johnson, S, Vasu, C, Solomon, S, Merson, M, Sikkema, K. *AIDS Behav*. 2007; 11: 491 - 504.

**Clinical impact and cost-effectiveness of antiretroviral therapy in India: Starting criteria and second-line therapy.** Freedberg, KA, Kumarasamy, N, Losina, E, Cecelia, AJ, Scott, CA, Divi, N, Flanigan, TP, Lu, Z, Weinstein, MC, Wang, B, Ganesh, AK, Bender, MA, Mayer, KH, Walensky, RP. *AIDS*. 2007; 21: S117-S128.

**Coinfection of hepatitis B and hepatitis C virus in HIV infected patients in South India.** Saravanan, S, Velu, V, Kumarasamy, N, Nandakumar, S, Murugavel, KG, Balakrishnan, P, Suniti, S, Thyagarajan, SP. *World J. Gastroenterol*. 2007; 13: 5015-5020.

**C-reactive protein in HIV-infected patients—could it be a marker of immunosuppression?** Muthu, S, Cecelia, AJ, Pulimi, S, Ameerda, L, Srinivas, CN, Solomon, SS, Narayan, A, Balakrishnan, P, Murugavel, KG, Solomon, S, Kumarasamy, N. *Clin. Chim. Acta*. 2007; 376: 246 - 247.

**Detection of pulmonary *Mycoplasma pneumoniae* infections in HIV-infected subjects using culture and serology.** Shankar, EM, Kumarasamy, N, Balakrishnan, P, Saravanan, S, Solomon, S, Vengatesan, A, Murugavel, KG, Rao, UA. *Int. J. Infect. Dis*. 2007; 11:232 - 238.

**Experience with the use of a first-line regimen of stavudine, lamivudine and nevirapine in patients in the TREAT Asia HIV observational database.** Zhou, J, Paton, NI, Ditangco, R, Chen, YM, Kamarulzaman, A, Kumarasamy, N, Lee, CK, Li, PC, Merati, TP, Phanuphak, P, Pujari, S, Vibhagool, A, Zhang, F, Chuah, J, Frost, KR, Cooper, DA, Law, MG. *HIV Med*. 2007; 8: 8 - 16.

**Exploring "Wine Shops" as a venue for HIV prevention interventions in urban India.** Sivaram, S, Johnson, S, Bentley, ME, Srikrishnan, AK, Latkin, CA, Go, VF, Solomon, S, Celentano, DD. *J. Urban Health*. 2007; 84: 563 - 576.

**Greater severity and extent of periodontal breakdown in 136 south Indian human immunodeficiency virus seropositive patients than in normal controls: a comparative study using community periodontal index of treatment needs.** Ranganathan, K, Magesh, KT, Kumarasamy, N, Solomon, S, Viswanathan, R, Johnson, NW. *Indian J. Dent. Res*. 2007; 18: 55 - 59.

**Oral lesions among persons with HIV disease with and without highly active antiretroviral therapy in southern India.** Umadevi, KM, Ranganathan, K, Pavithra, S, Hemalatha, R, Saraswathi, TR, Kumarasamy, N, Solomon, S, Greenspan, JS. *J. Oral Pathol. Med*. 2007; 36: 136 - 141.

**Sexual behaviors of individuals with HIV living in south India: a qualitative study.** Srikrishnan, AK, Hendriksen, E, Vallabhaneni, S, Johnson, SL, Raminani, S, Kumarasamy, N, Hobsen, J, Solomon, S, Mayer, KH, Safren, SA. *AIDS Educ. Prev*. 2007; 19: 334 - 345.

**Weight and body shape changes in a treatment-naive population after 6 months of nevirapine-based generic highly active antiretroviral therapy in south India.** Saghayam, S, Kumarasamy, N, Cecelia, AJ, Solomon, S, Mayer, K, Wanke, C. *Clin. Infect. Dis*. 2007; 44: 295 - 300.

## Invitation for Contributors

We welcome your contribution towards YRG CARE. Donations to YRG CARE are eligible for tax deductions under **Section 80G** of the Income Tax Act. The Foundation is registered with the Ministry of Home Affairs to receive Foreign Contributions under the Foreign Contributions Regulation Act (**FCRA**) vide registration No. 75900630/12 July 1991. Please mail us with the subject head 'Donations' with your contact details.

## Ask the Experts

Readers are invited to send their queries on HIV/AIDS, which will be answered by experts from YRG CARE in the subsequent issue.

### News

#### COST-EFFECTIVE HIV DIAGNOSTIC SERVICES

YRG CARE offers certified, quality assured and cost-effective HIV monitoring laboratory tests; CD4+ T-Cell Count (Rs.250/-) and HIV-1 Drug Resistance Genotyping Assay (Rs.4000/- for RT drugs, Rs.6000/- for RT and PI drugs).

The laboratory also offers various internationally certified STD testing for the prevention trials/research studies. Contact: [hanas@dtiassociates.org](mailto:hanas@dtiassociates.org)

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Should you wish to send us your comments/ suggestions/ email subscription regarding this newsletter, please write to us.

### Editor-in-chief / Publisher

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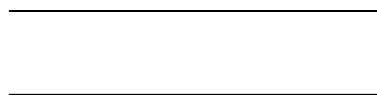
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